

Claims 1-3 stand rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-4 of US 6,171,801. A terminal disclaimer is enclosed.

Claims 1-3 stand rejected under the judicially created doctrine of obviousness-type double patenting over claims 1, 2, 4, 5, 10, 11, 26 and 27 of US 6,159,698. A terminal disclaimer is enclosed.

#### **Rejection under 35 U.S.C. Section 103(a)**

The Examiner maintained the rejection of claims 1-3 over Tabachnick et al. in view of Khanna et al. Applicants have argued that Tabachnick teaches away from using Applicants method and thus one skilled in the art would not even look to Khanna. The Examiner disagrees that Tabachnick teaches away from the claimed invention stating that while Tabachnick demonstrates a reduction in relative affinity is not equivalent to absence of affinity. The Examiner states that instead of being discouraged Khanna expressly taught the successful use of the specific substituted benzoic acid, methoxybenzoic acid as a releasing agent for releasing a ligand from a complex. Thus, the Examiner asserts that this is prima facie evident that Tabachnick et al does not teach away from the present invention.

Applicants respectfully disagree that Tabachnick does not teach away from the present invention - which is a method of releasing **endogenous proteins** from a ligand. The ortho derivative in table II lists a Relative affinity of 30, substantially less than most of the other derivatives listed. Further, Tabachnick et al specifically states : "However, a benzoate derivative having a halogen (or nitro) substituent ortho to the carboxyl group exhibits a reduced affinity for HAS compared to a similarly substituted phenol . . ." See page 471, col. 1 last paragraph. Thus, Applicants again submit that Tabachnick teaches away from using the present invention and one skilled in the art would not look to Tabachnick for guidance. Furthermore, Khanna describes releasing a beta cyclodextrin from digoxin. Cyclodextrin is not an endogenous protein, or even a protein. Beta cyclodextrin is a carbohydrate that provides space in the interior of

a single molecule for the inclusion of guest molecules. It is not an endogenous protein that forms a complex with a ligand. See *The Encyclopedia of Chemical Terminology (3<sup>rd</sup> Edition) Vol. 6*. A copy has been enclosed for the Examiner's convenience.

5 In conclusion Applicants submit that the present invention is not obvious over the combination cited by the Examiner.

Applicants ask that the contact the undersigned at the phone number listed below if the Examiner believes that an interview would clarify any issue.

10 Respectfully submitted,



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